STN-Structure Search 1-30-06

10/524,922

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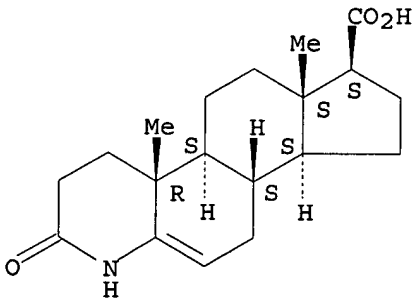
L9 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:236766 CAPLUS
DOCUMENT NUMBER: 144:71434
TITLE: Studies on synthesis of finasteride
AUTHOR(S): Sheng, Rong; Hu, Yongzhou
CORPORATE SOURCE: College of Pharmaceutical Science, Zhejiang University, Hangzhou, Zhejiang Province, 310031, Peop. Rep. China
SOURCE: Zhongguo Yaoxue Zazhi (Beijing, China) (2004), 39(3), 226-228
CODEN: ZYZAEU; ISSN: 1001-2494
PUBLISHER: Zhongguo Yaoxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The ring A of initial material 3-oxo-4-androstene-17β-carboxylic acid was opened with KMnO4-NaIO4. Then the product was reacted with NH3 and hydrogenated with Pd/C to get 3-oxo-4-aza-5α-androsta-17β-carboxylic acid, which was esterified with anhydrous CH3OH, dehydrogenated with DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone)/BSTFA [bis(trimethylsilyl) trifluoroacetamide], and reacted with t-butylamine and ethylmagnesium bromide to get finasteride. The structures of all the intermediates and finasteride were verified by IR, 1HNMR and MS. This method was successful without using those expensive reagents such as PtO2, (PhSeO)2O and 2,2'-dipyridyl disulfide. The column chromatog. was not necessary for all steps. The yield of finasteride reached 44.3%, and it was much higher than the reported yield.

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(in synthesis of finasteride)

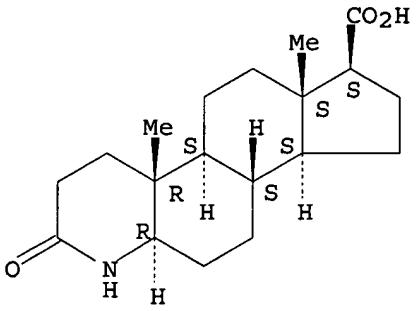
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

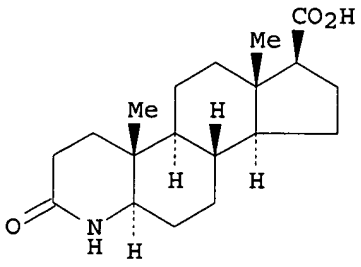
Absolute stereochemistry.



L9 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:162674 CAPLUS
DOCUMENT NUMBER: 140:199498
TITLE: Method for the selective preparation of a 3-oxo-4-aza-5a-androstane derivative
INVENTOR(S): Moon, Young-ho; Lee, Kyung-ik; Park, Gha-seung; Park, Chul-hyun; Lee, Jae-cheol; Lee, Gwan-sun; Chang, Young-kil
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004016595	A1	20040226	WO 2003-KR1629		20030813
W: AU, CA, CN, HU, IN, JP, US					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
EP 1539703	A1	20050615	EP 2003-788151		20030813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK					
JP 2006501221	T2	20060112	JP 2004-528926		20030813
US 2006019979	A1	20060126	US 2005-524922		20050215
PRIORITY APPLN. INFO.:			KR 2002-48784	A	20020819
			WO 2003-KR1629	W	20030813

GI



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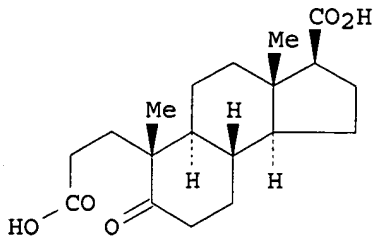


II

AB This invention relates to a method for selectively preparing 3-oxo-4-aza-5α-androstane derivative I, a precursor of finasteride, by heating 3-oxo-4-aza-5-androstene in a mixture of formic acid and an alkanediol in the presence of zinc. Thus, oxidative ring cleavage of

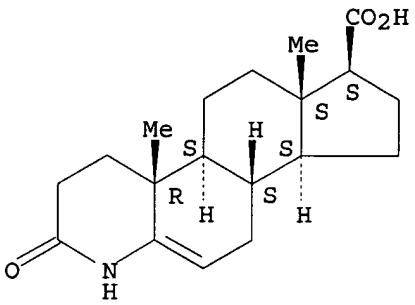
3-oxo-4-androstene-17β-carboxylic acid using sodium metaperiodate, potassium permanganate, and sodium carbonate in tert-butanol gave 3,5-secoandrostane II in 86% yield. Ring cleaved androstane II then underwent an intramol. cyclocondensation reaction by refluxing for 12 h using an ethanolic ammonia solution and ethylene glycol to form 3-oxo-4-aza-5-androstene-17β-carboxylic acid in 70% yield, which was subsequently hydrogenated by heating for 8 h at 100-105° using formic acid, ethylene glycol and zinc to give the desired finasteride precursor I in 81% yield.

IT **103335-54-2P**, 3-Oxo-4-aza-5-androstene-17β-carboxylic acid
RL: IMF (Industrial manufacture); **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of 3-oxo-4-aza-5α-androstane, a finasteride precursor, via a zinc/formic acid/alkanediol mediated olefin hydrogenation)

RN 103335-54-2 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

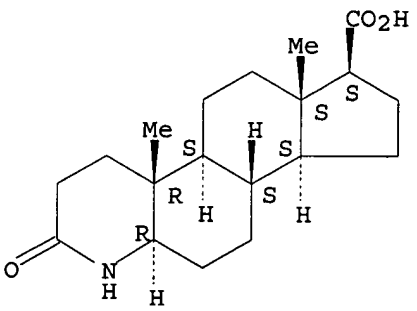


IT **103335-55-3P**, 3-Oxo-4-aza-5α-androstane-17β-carboxylic acid
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(process for preparation of 3-oxo-4-aza-5α-androstane, a finasteride precursor, via a zinc/formic acid/alkanediol mediated olefin hydrogenation)

RN 103335-55-3 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

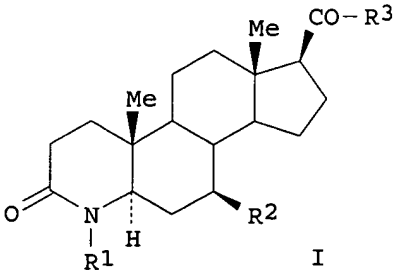


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:449695 CAPLUS
DOCUMENT NUMBER: 137:20508
TITLE: Preparation of 3-oxo-4-azasteroids via stereoselective hydrogenation
INVENTOR(S): Davis, Roman; Millar, Alan; Sterbenz, Jeffrey Thomas
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002046207	A2	20020613	WO 2001-US48173		20011102
WO 2002046207	A3	20030320			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2427709	AA	20020613	CA 2001-2427709		20011102
AU 2002041624	A5	20020618	AU 2002-41624		20011102
EP 1335930	A2	20030820	EP 2001-988307		20011102
EP 1335930	B1	20041013			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001015089	A	20031007	BR 2001-15089		20011102
JP 2004515505	T2	20040527	JP 2002-547944		20011102
AT 279429	E	20041015	AT 2001-988307		20011102
PT 1335930	T	20050131	PT 2001-988307		20011102
NZ 525168	A	20050324	NZ 2001-525168		20011102
ES 2230383	T3	20050501	ES 2001-1988307		20011102
ZA 2003002560	A	20040401	ZA 2003-2560		20030401
US 2004049042	A1	20040311	US 2003-415922		20030505
US 6794508	B2	20040921			
HK 1058799	A1	20050527	HK 2004-100269		20040114
PRIORITY APPLN. INFO.:			GB 2000-26876	A	20001103
			WO 2001-US48173	W	20011102

OTHER SOURCE(S): CASREACT 137:20508; MARPAT 137:20508
GI



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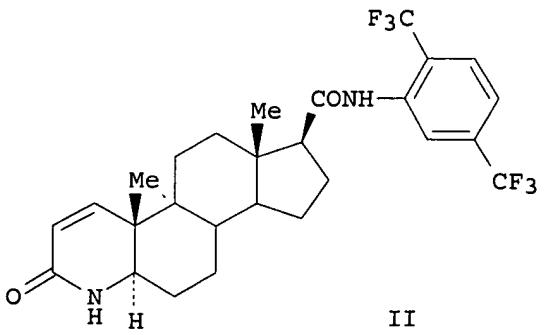


II

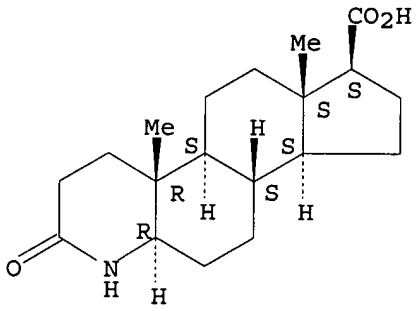
AB An improved process for preparing steroids, such as 3-oxo-4-azasteroids of formula I [R1 = H, OH, alkyl, aryl, heteroarom. group; R2 = H, alkyl, aryl, heteroarom. group; R3 = H, OH, alkyl, alkoxy, aryl, (substituted) NH2, etc.], is described. Compds. of this type are known to be useful in the preparation of compds. having 5α-reductase inhibitor activity. The process comprises the hydrogenation of the corresponding steroid alkene in the presence of ammonium acetate, ammonium formate, and/or ammonium propionate and an appropriate catalyst. Thus, 3-oxo-4-aza-5-androstene-17β-carboxylic acid (preparation given) was hydrogenated with ammonium acetate and PtO2 to give 3-oxo-4-aza-5α-androstane-17β-carboxylic acid with a high α:β ratio. 3-Oxo-4-aza-5α-androstane-17β-carboxylic acid was reacted with DDQ and bis(trimethylsilyl)trifluoroacetamide (BSTFA), then SOCl2 and 2,5-bis(trifluoromethyl)aniline to give II.

IT **103335-55-3P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of 3-oxo-4-azasteroids via stereoselective hydrogenation)

RN 103335-55-3 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

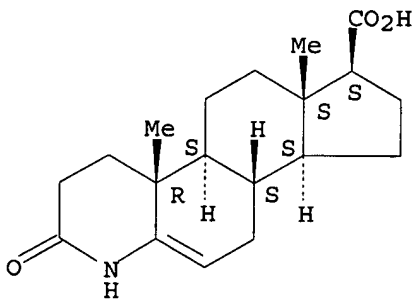


IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-oxo-4-azasteroids via stereoselective hydrogenation)

RN 103335-54-2 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



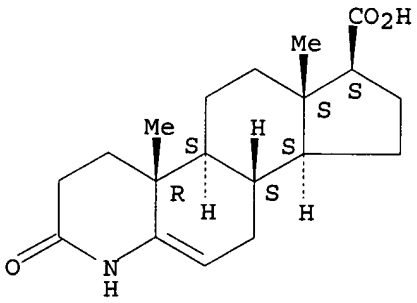
L9 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:245625 CAPLUS
DOCUMENT NUMBER: 137:155095
TITLE: Synthesis of Finasteride
AUTHOR(S): Li, Xiao-jun; Fang, Fang; Wang, Xiao-ji; Chen, Li-gong
CORPORATE SOURCE: School of Pharmaceutical Science and Technology, Tianjin University, Tianjin, 300072, Peop. Rep. China
SOURCE: Transactions of Tianjin University (2001), 7(4), 286-289
CODEN: TTUNEB; ISSN: 1006-4982
PUBLISHER: Tianjin University
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:155095

AB As a kind of substrate competition-type 5α-reductase inhibitor, Finasteride is a promising medicine used in the clin. treatment of benign prostatic hyperplasia (BPH). In this paper, a new route for the synthesis of Finasteride from pregnenolone was proposed. Thus, pregnenolone was converted to Finasteride in 10 steps, i. e., via ammoniumation, methoxylation, Oppenauer oxidation, hydrolyzation, cleavage of Δ4-double bond by oxidation, ring closure by ammonia, hydrogenation of Δ5-double bond, esterification with methanol, dehydrogenation of 1, 2-position in A-ring and Bodroux reaction. In this route, expensive reagent 2, 2'-dipyridyl-disulfide commonly used in previous literature was avoided. All of the desired compds. were characterized by MS or/and NMR. The overall yield of Finasteride was 13.67% based on pregnenolone.

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(synthesis of Finasteride)

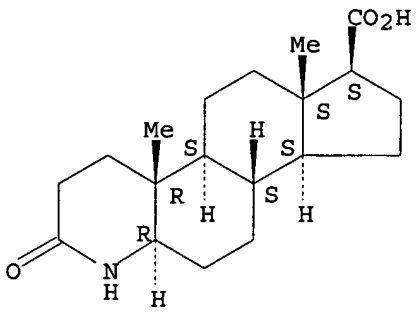
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

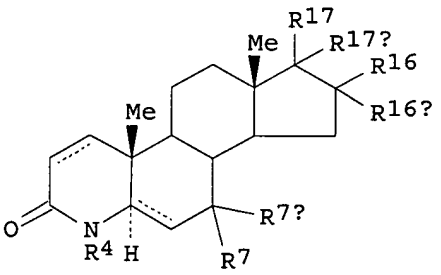


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:776029 CAPLUS
DOCUMENT NUMBER: 128:61680
TITLE: Preparation of substituted 4-aza-3-oxo-steroids for use as 5α-reductase inhibitors
INVENTOR(S): Durette, Philippe L.; Hagmann, William; Rasmusson, Gary H.; Tolman, Richard L.; Kopka, Ihor E.; Sahoo, Soumya P.; Esser, Craig K.; Steinberg, Nathan G.; Graham, Donald W.; Witzel, Bruce E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 139 pp., Cont.-in-part of U.S. Ser. No. 886,537, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5693809	A	19971202	US 1995-338571	19950512
PRIORITY APPLN. INFO.:			US 1992-886537 B2	19920520

OTHER SOURCE(S): MARPAT 128:61680
GI



I

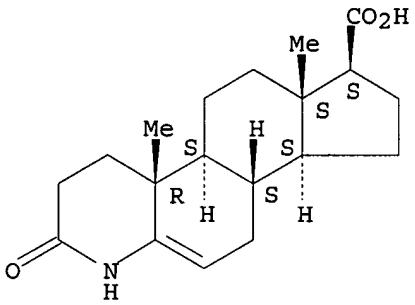
AB Steroids such as 4-aza-5α-androstan-ones I [1,2-, 5,6-saturated or unsatd.; R4 = H, Me, Et; R7 = R7a = H, OH, alkyl, alkenyl, carbamoyloxy, carboxy, etc.; R7R7a = oxo, cycloalkyl, etc.; R16 = R16a = H, alkyl; R16R16a = cyloalkenyl; R17 = R17a = H, acyl, carbamoyl, aminoalkyl, alkyl, etc.; R17R17a = oxo, etc.] were prepared as 5α-reductase inhibitors for treatment of hyperandrogenic conditions. Thus, 4-methyl-17β-(trimethylacetamido)-5α-4-azaandrostan-3-one was prepared via

oximation of 4-methyl-3-oxo-5α-4-azaandrostan-17-carboxaldehyde, hydrogenation to form the corresponding amine followed by N-acylation with Me3CCO2Cl. The prepared compds. were tested for inhibition of human prostatic and scalp 5α-reductase, however, activities for specific compds. were not presented.

IT **103335-54-2P 103335-55-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **RCT (Reactant)**; SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of substituted 4-aza-3-oxo-5α-steroids for use as 5α-reductase inhibitors)

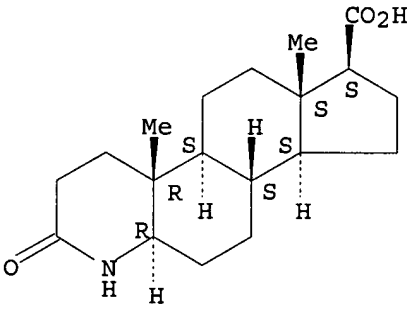
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:54919 CAPLUS
DOCUMENT NUMBER: 126:144437
TITLE: Synthesis of finasteride, a new drug of the treatment of benign prostatic hyperplasia
AUTHOR(S): Zheng, Jinhong; Xu, Fang; Liao, Qingjiang
CORPORATE SOURCE: Res. Cent. Drugs Family Planning, China Pharmaceutical univ., Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (1996), 6(3), 203-206

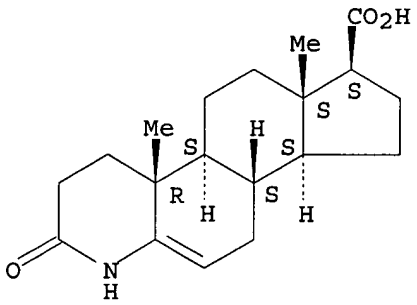
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Finasteride was prepared in 10 steps from pregnenolone. The synthetic method of some key intermediates was improved to suit the need of industrial production

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of finasteride, for treatment of benign prostatic hyperplasia)

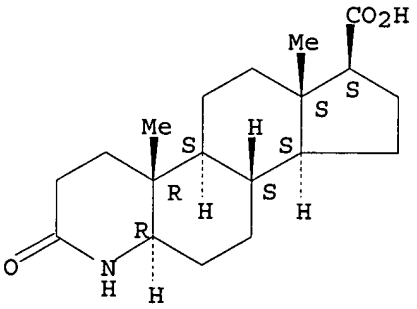
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



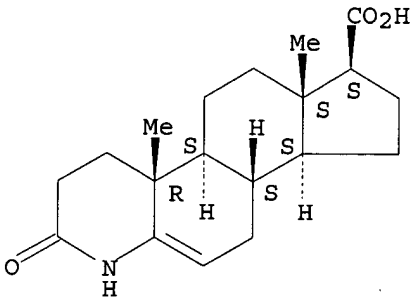
L9 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:1003500 CAPLUS
DOCUMENT NUMBER: 124:44623
TITLE: Synthesis of 5,6,6-[2H3]finasteride and quantitative determination of finasteride in human plasma at picogram level by an isotope-dilution mass spectrometric method
AUTHOR(S): Guarna, A.; Danza, G.; Bartolucci, G.; Marrucci, A.; Dini, S.; Serio, M.
CORPORATE SOURCE: Dipartimento di Chimica Organica Ugo Schiff e Centro di Studio Sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, Universita di

Firenze, Via G. Capponi, 9, I-50124, Firenze, Italy
SOURCE: Journal of Chromatography, B: Biomedical Applications (1995), 674(2), 197-204
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Finasteride is a potent inhibitor of the enzyme steroid 5α-reductase now approved as a drug for the treatment of benign prostatic hyperplasia. The authors describe an original method for the quant. determination of finasteride at picogram level in human plasma by isotope-dilution gas chromatog. mass spectrometry. 5,6,6-[2H3]Finasteride was prepared with a high ratio of trideuteration (finasteride/[2H3]finasteride = 0.007) allowing its optimal use as internal standard Plasma samples were purified in a single-step procedure on solid-phase extraction C18 columns with a recovery ≥90%. Samples were injected in the GC-MS instrument without any derivatization and the min. detection level of finasteride was 50 pg with a signal-to-noise ratio of 6:1. The coeffs. of variation for the 5 and 10 ng/mL (plasma) concns. were 5.8% and 4%, resp. The method has been applied to the determination of the plasma pharmacokinetic of finasteride in five male volunteers treated with a single 5-mg dose of the drug, affording kinetic parameters which are in good agreement with the values previously reported with a different methodol. The present method results accurate, specific, sensible and reliable for a routinely determination of finasteride at picogram levels.

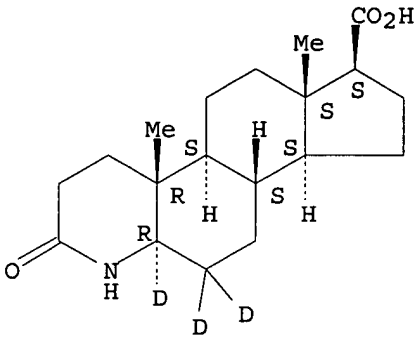
IT **103335-54-2**
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(deuteration-reduction of)
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **172302-43-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and dehydrogenation of)
RN 172302-43-1 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-11-d-7-carboxylic acid, hexadecahydro-11,11a-d2-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

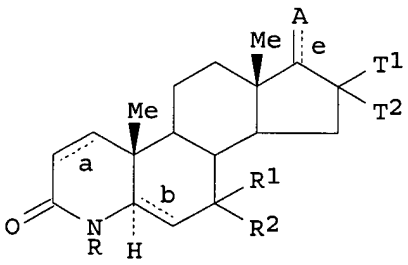
Absolute stereochemistry.



L9 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:266948 CAPLUS
DOCUMENT NUMBER: 122:56297
TITLE: preparation of substituted 4-aza-5a-androstanones as 5α-reductase inhibitors
INVENTOR(S): Durette, Philippe L.; Hagmann, William; Rasmusson, Gary H.; Tolman, Richard L.; Kopka, Ihor E.; Sahoo, Soumya P.; Esser, Craig K.; Steinberg, Nathan G.; Graham, Donald W.; Witzel, Bruce E.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 533 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323039	A1	19931125	WO 1993-US4734	19930518
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342519	A1	19931213	AU 1993-42519	19930518
PRIORITY APPLN. INFO.:			US 1992-886537	A2 19920520
			WO 1993-US4734	A 19930518

OTHER SOURCE(S): MARPAT 122:56297
GI



I

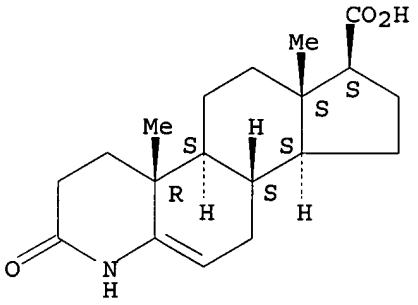
AB 4-Aza-5α-androstan-3-ones [I; R = H, Me, Et; T1, T2 = H, C1-6 alkyl, T1T2 = C1-6 alkylidene; R1, R2 = H, C1-4 alkyl, C2-4 alkenyl, CO2H, OH, CH2CO2H, carbamoyloxy, etc., R1R2 = O; A = (substituted) hydrocarbyl, carbamoyl, etc.; a, b, e = single or double bond] and related compds.,

effective at 0.01-7 mg/kg as 5α-reductase inhibitors in treating benign prostatic hypertrophy, prostatitis, prostatic carcinoma, hyperandrogenic conditions, etc., are prepared Thus, oximation of 4-methyl-3-oxo-4-aza-5α-androstane-17β-carboxaldehyde and subsequent reduction by H over PtO2 gave the corresponding 17β-(aminomethyl) derivative Acylation of this aminomethyl compound with MeO2C(CH2)7COCl in pyridine/CH2Cl2 gave 17β-[[[8-(methoxycarbonyl)octanoyl]amino]methyl]-4-methyl-4-aza-5α-androstan-3-one.

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of azaandrostanones with 5α-reductase inhibiting activity)

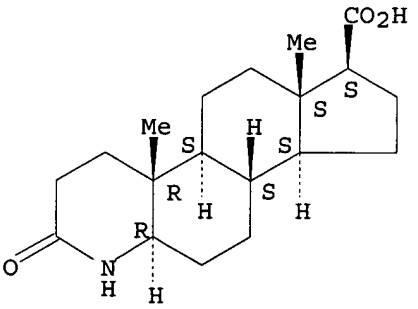
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:73747 CAPLUS
DOCUMENT NUMBER: 122:133510
TITLE: Partial synthesis of N-(1,1-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide
AUTHOR(S): Lorenc, Ijubinka; Pavlovic, Vladimir; Bondarenko-Gheorghiu, Lidija; Mihailovic, Mihailo L. J.
CORPORATE SOURCE: Fac. Chem., Univ. Belgrade, Belgrade, YU-11001,

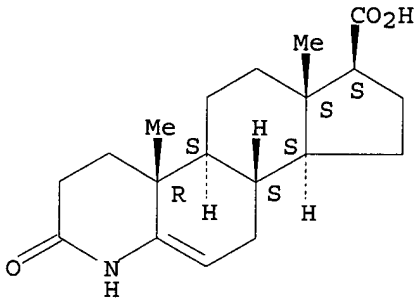
Yugoslavia
SOURCE: Journal of the Serbian Chemical Society (1993), 58(12), 991-5
CODEN: JSCSEN; ISSN: 0352-5139
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A partial synthesis of N-(1,1-dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide starts from 21-hydroxypregn-4-ene-3,20-dione and involves the oxidative degradation of the 17β-function to the 17β-carboxylic group, oxidative fragmentation in ring A leading to the 3,5-seco-4-nor-dicarboxylic acid, ring A closure to the Δ5-unsatd. lactam, catalytic hydrogenation of the Δ5-olefinic double bond, introduction of the amide function,; and dehydrogenation with formation of the Δ1-double bond. The overall yield of this six-step synthesis is approx. 20%.

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of azaandrostenecarboxamide)

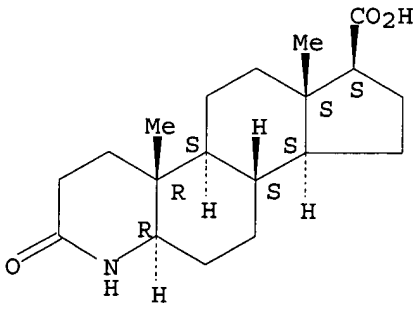
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:570583 CAPLUS
DOCUMENT NUMBER: 121:170583
TITLE: Combination method for treating patterned alopecia

with 17-β-N-substituted-carbamoyl-4-aza-5-α-androst-1-en-3-ones and minoxidil

INVENTOR(S): Rasmusson, Gary H.; Tolman, Richard L.
PATENT ASSIGNEE(S): Merck and Co. Inc., USA

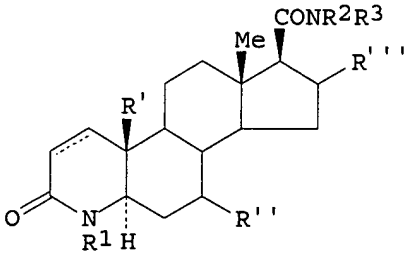
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9415602	A1	19940721	WO 1994-US176	19940105
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9460834	A1	19940815	AU 1994-60834	19940105

PRIORITY APPLN. INFO.: US 1993-1373 A2 19930107
WO 1994-US176 W 19940105

OTHER SOURCE(S): MARPAT 121:170583

GI



I

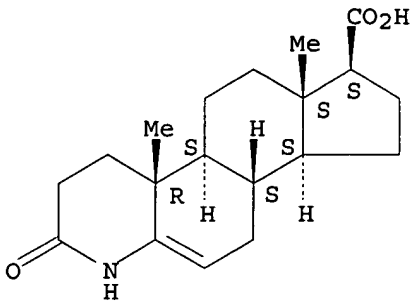
AB 17β-N-substituted-carbamoyl-4-aza-5-α-androst-1-en-3-ones I, [dotted line = double bond, when present; R1, R3 = H, Me, Et; R2 = (branched) (substituted) alkyl, cycloalkyl, aralkyl of 1-12 C, monocyclic aryl optionally containing ≥1 lower alkyl substituents of 1-2 C and/or ≥1 halogens; R', R'', R''' = H, Me; with the proviso that R2 is not tert-Bu where R1 and R3 are H], are useful in combination therapy with minoxidil for treating patterned alopecia, male pattern baldness, female pattern alopecia, alopecia senilis or alopecia areata. Preparation of selected I are included, as are formulations.

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction of, for carbamoylazaandrostenone derivative preparation for patterned alopecia treatment)

RN 103335-54-2 CAPLUS

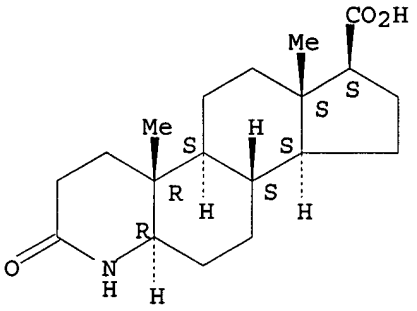
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



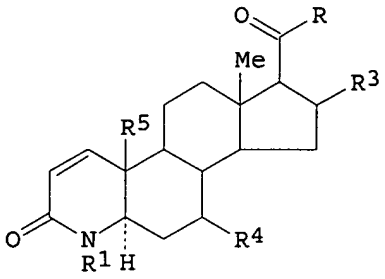
L9 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:560644 CAPLUS
DOCUMENT NUMBER: 119:160644
TITLE: Preparation of 17β-carbamoyl-4-aza-5α-androst-1-en-3-ones as testosterone 5α-reductase inhibitors for the prevention of prostatic carcinoma
INVENTOR(S): Gormley, Glenn J.; Stoner, Elizabeth
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 547691	A1	19930623	EP 1992-203857	19921210
EP 547691	B1	19970319		
R: CH, DE, FR, GB, IT, LI, NL				
CA 2084799	AA	19930618	CA 1992-2084799	19921208
CA 2084799	C	20030128		
JP 05255381	A2	19931005	JP 1992-329359	19921209
JP 2538489	B2	19960925		
US 6268376	B1	20010731	US 1994-364072	19941227
LV 12067	B	19980820	LV 1998-34	19980303
US 2001049376	A1	20011206	US 2001-875381	20010606
US 6432971	B2	20020813		
PRIORITY APPLN. INFO.:			US 1991-808510 A	19911217

US 1993-16474 B1 19930210
US 1994-190769 B1 19940202
US 1994-364072 A3 19941227

OTHER SOURCE(S): MARPAT 119:160644

GI



I

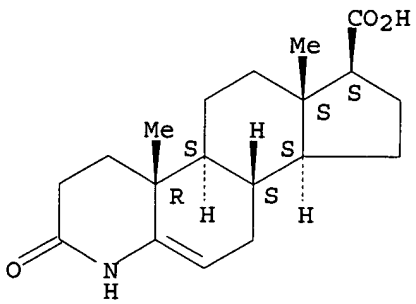
AB Title compds. [I; R = NHR2; R1 = H, Me, Et; R2 = (cyclo)alkyl, aralkyl, (halo)aryl, alkylaryl; R3, R5 = H or Me; R4 = H or β-Me] were prepared as testosterone 5α-reductase inhibitors (no data). Thus, Me 3-oxo-4-aza-5α-androstane-17-carboxylate was treated with [PhSe(O)]2O and the product N-methylated to give, after saponification, I (R1 = R5 = Me, R3 = R4 = H) (II; R = OH). The latter was esterified by 2,2'-dipyridyl disulfide and the thioester product amidated by Me3CNH2 to give II (R = NHCMe3). Use of I for manufacture of medicaments for preventing prostatic carcinoma in asymptomatic patients is claimed.

IT **103335-54-2P 103335-55-3P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction of, in preparation of testosterone 5α-reductase inhibitor)

RN 103335-54-2 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

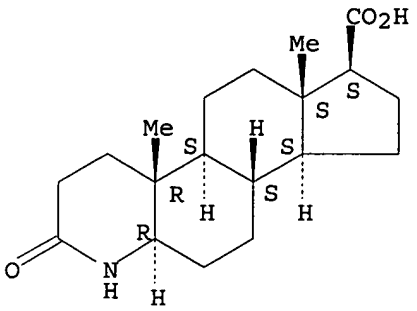
Absolute stereochemistry.



RN 103335-55-3 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:213352 CAPLUS
DOCUMENT NUMBER: 118:213352
TITLE: Pharmaceutical combination for the treatment of prostatic cancer containing a 5 alpha reductase inhibitor and an antiandrogen
INVENTOR(S): Gormley, Glenn J.; Stoner, Elizabeth
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 286 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

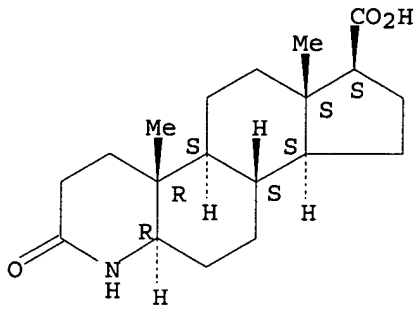
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9216233	A1	19921001	WO 1992-US2213		19920319
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD					
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG					
AU 9216802	A1	19921021	AU 1992-16802		19920319
ZA 9202012	A	19921125	ZA 1992-2012		19920319
US 5994362	A	19991130	US 1995-459063		19950602
PRIORITY APPLN. INFO.:			US 1991-672506	A	19910320
			US 1992-846154	A	19920311
			WO 1992-US2213	A	19920319
			US 1993-94950	B1	19931227

OTHER SOURCE(S): MARPAT 118:213352

AB Prostatic cancer treatment involved combination therapy of a 5α-reductase inhibitor, i.e, a 17β-substituted 4-azasteroid, or nonazasteroid, 17β-acyl-3-carboxyandrost-3,5-diene, benzoylaminophenoxybutanoic acid derivative, fused benz(thio)amide or cinnamoylamide derivative, aromatic 1,2-diethers or thioether, aromatic o-acylaminophenoxyalkanoic acids, o-thioalkylacylaminophenoxyalkanoic acids, and particularly finasteride, in combination with an antiandrogen, i.e., flutamide. A large number of examples of steroids preparation was given including Me 3-oxo-4-aza-5α-androst-1-ene-17β-carboxylate which was prepared by dehydrogenation of of the corresponding 5α-androstane derivative Tablets were prepared containing 50 mg 4-[2-[4-[1-(4-isobutylphenyl)ethoxy]-2,3-dimethylbenzoylamino]phenoxy]butanoic acid.

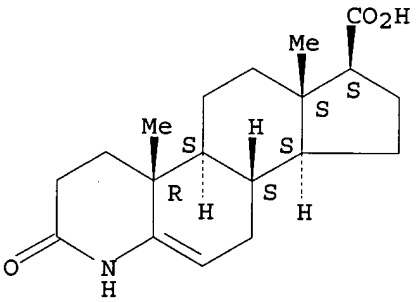
IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and amidation of)
RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:102309 CAPLUS
DOCUMENT NUMBER: 118:102309
TITLE: Pharmaceutical combination for the treatment of prostatic hyperplasia, containing a 5α-reductase inhibitor and an α1-adrenergic receptor blocker, and synthesis of some 5α-reductase inhibitors
INVENTOR(S): Gormley, Glenn J.; Stoner, Elizabeth
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9216213	A1	19921001	WO 1992-US2258	19920319

W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN,

GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG					
IL 101243	A1	19991222	IL 1992-101243		19920316
NZ 260737	A	20000728	NZ 1992-260737		19920316
CA 2104793	AA	19920921	CA 1992-2104793		19920319
CA 2104793	C	20040622			
AU 9217514	A1	19921021	AU 1992-17514		19920319
AU 666846	B2	19960229			
ZA 9202010	A	19921125	ZA 1992-2010		19920319
EP 576603	A1	19940105	EP 1992-910266		19920319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 06506227	T2	19940714	JP 1992-509435		19920319
HU 66273	A2	19941128	HU 1993-2624		19920319
RO 113613	B1	19980930	RO 1993-1253		19920319
RU 2125879	C1	19990210	RU 1993-55133		19920319
SG 80530	A1	20010522	SG 1996-3649		19920319
CZ 292712	B6	20031217	CZ 1993-1933		19920319
SK 284381	B6	20050204	SK 1993-1006		19920319
NO 9303327	A	19931117	NO 1993-3327		19930917
NO 305635	B1	19990705			
US 5753641	A	19980519	US 1995-428595		19950425
US 6046183	A	20000404	US 1998-27105		19980220
PRIORITY APPLN. INFO.:			US 1991-672511	A	19910320
			US 1992-846153	A	19920311
			NZ 1992-241979	A1	19920316
			WO 1992-US2258	A	19920319
			US 1993-22805	B1	19930222
			US 1994-201063	B1	19940224
			US 1995-428595	A1	19950425

OTHER SOURCE(S): MARPAT 118:102309

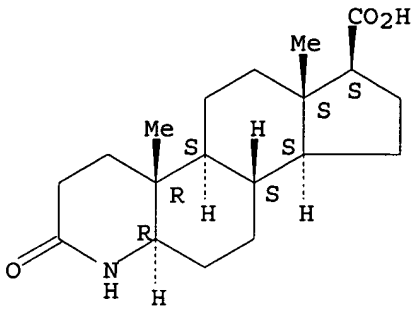
AB A method of treating benign prostatic hyperplasia is claimed, in which a 5α-reductase inhibitor selected from a variety of types is administered in combination with an α1-adrenergic receptor blocker (no examples or data). In particular, administration of 5 mg finasteride and 5-10 mg terazosin in one daily dose is preferred. A large number of examples cover synthesis of 5α-reductase inhibitors, including 17β-substituted steroids and 4-azasteroids, benzoylaminophenoxybutanoic acids, etc. For example, Me 3-oxo-4-aza-5α-androstane-17β-carboxylate underwent dehydrogenation to introduce Δ1 double bond, N-methylation with NaH and MeI, saponification, conversion to an S-(2-pyridyl) thioester, and amidation with tert-BuNH2, to give N-(tert-butyl)-4-methyl-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide, i.e. the 4-Me derivative of finasteride.

IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and amidation of)

RN 103335-55-3 CAPLUS

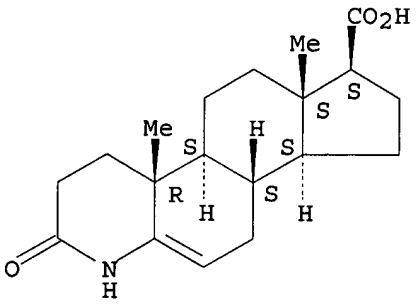
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

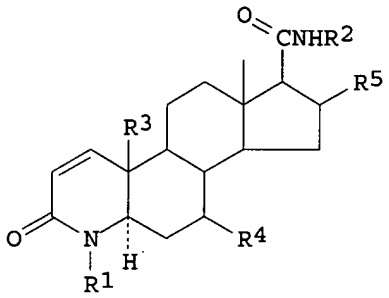
Absolute stereochemistry.



L9 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:135565 CAPLUS
DOCUMENT NUMBER: 110:135565
TITLE: Treatment of prostatic carcinoma with 17β-N-monosubstituted carbamoyl-4-aza-5α-androst-1-en-3-ones
INVENTOR(S): Rasmusson, Gary H.; Reynolds, Glen F.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 285383	A2	19881005	EP 1988-302808	19880330
EP 285383	A3	19900912		
EP 285383	B1	19940316		
R: CH, DE, FR, GB, IT, LI, NL				
CA 1302276	A1	19920602	CA 1988-563183	19880331
PRIORITY APPLN. INFO.:			US 1987-34808 A	19870403
OTHER SOURCE(S):	MARPAT 110:135565			

GI



I

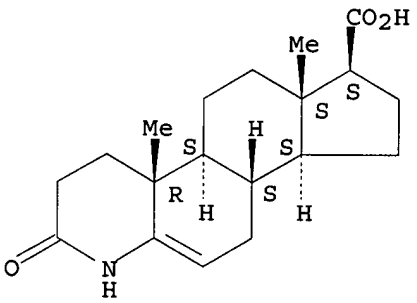
AB The title compds. (I; R1 = H, Me, Et; R2 = branched alkyl; R3 = H, Me; R4 = H, β-Me; R5 = H, α- or β-Me) is a drug for the treatment of prostatic carcinoma (no data). A suspension of Me 3-oxo-4-aza-5α-androstane-17-carboxylate and benzeneselenic anhydride in C6H5Cl was refluxed for 2 h to give Me 3-oxo-4-aza-5α-androst-1-ene-17β-carboxylate. This was stirred with NaH in dry DMF for 15 min, followed by addition of MeI to give the corresponding Me ester, which was refluxed with KOH in aqueous MeOH, followed by stirring with Ph3P and 2,2'-dipyridyl disulfide in PhMe to give S-(2-pyridyl)-4-methyl-3-oxo-4-aza-5α-androst-1-ene-17β-thiocarboxylate. This was treated with anhydrous tert-BuNH2 in THF to give N-tert-butyl-4-methyl-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide.

IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)

RN 103335-54-2 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

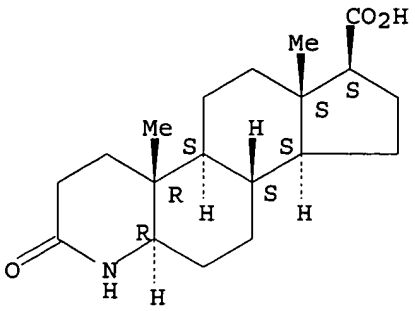


IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction with trimethylpentylamine)

RN 103335-55-3 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

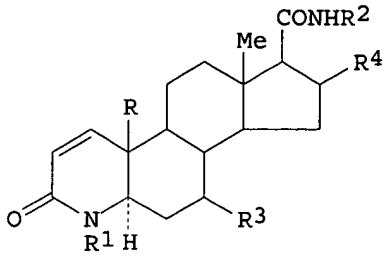
Absolute stereochemistry.



L9 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:101528 CAPLUS
DOCUMENT NUMBER: 110:101528
TITLE: Treatment of androgenic alopecia with 17β-monosubstituted-carbamoyl-4-aza-5α-androst-1-en-3-ones
INVENTOR(S): Rasmusson, Gary H.; Reynolds, Glen F.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 285382	A2	19881005	EP 1988-302807	19880330
EP 285382	A3	19900912		
EP 285382	B1	19940413		
R: CH, DE, FR, GB, IT, LI, NL				
CA 1302277	A1	19920602	CA 1988-563185	19880331
US 5571817	A	19961105	US 1993-94815	19930720
US 5567708	A	19961022	US 1995-455464	19950531
PRIORITY APPLN. INFO.:			US 1987-34806 A	19870403
			US 1984-584062 B1	19840227
			US 1985-800623 A2	19851121
			US 1988-198708 B1	19880519
			US 1989-370142 B1	19890621
			US 1990-545676 B1	19900628
			US 1991-698374 B1	19910509
			US 1992-927256 B1	19920807
			US 1993-16476 B1	19930210
			US 1993-94815 A1	19930720

OTHER SOURCE(S): MARPAT 110:101528
GI



I

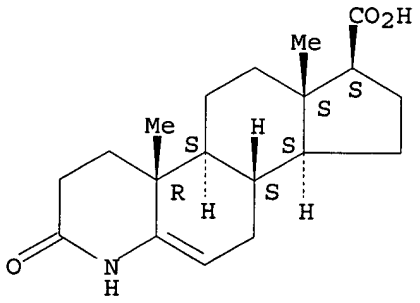
AB The title compds. I (R = H, Me; R1 = H, Me, Et; R2 = C3-12 branched alkyl; R3 = H, β-Me; R4 = H, α-Me, β-Me) are prepared as agents for treatment of androgenic alopecia. Me 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17β-carboxylate (preparation given) was hydrolyzed by refluxing with aqueous KOH for 4 h, to give the free acid, which was stirred in a suspension of Ph3P and 2,2'-dipyridyl disulfide in toluene to give S-(2-pyridyl) 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17β-thiocarboxylate. This was suspended in THF and tert-BuNH2 was bubbled through the suspension, to give N-tert-butyl-4-methyl-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide (II). A cream shampoo comprised II 0.1, Na laureth sulfate 65.0, glyceryl tribehenate 2.0, hydrolyzed collagen 1.0, lauric diethanolamide 5.0 and H2O 26.9% by weight

IT **103335-54-2P**
RL: **RCT (Reactant)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and catalytic hydrogenation of)

RN 103335-54-2 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

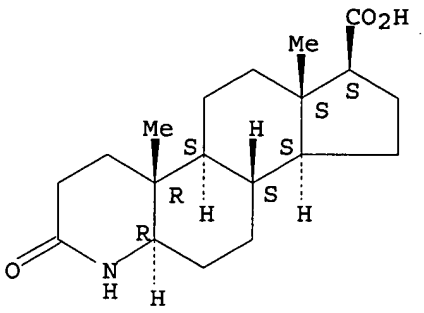


IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction of, with hydroxybenzotriazole)

RN 103335-55-3 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

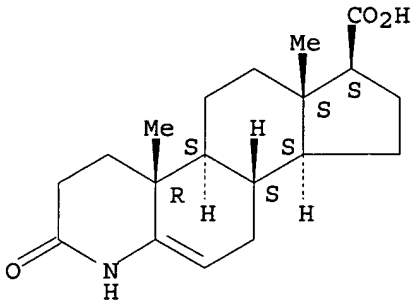


L9 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:33371 CAPLUS
DOCUMENT NUMBER: 106:33371
TITLE: Azasteroids: structure-activity relationships for inhibition of 5α-reductase and of androgen receptor binding
AUTHOR(S): Rasmusson, Gary H.; Reynolds, Glenn F.; Steinberg, Nathan G.; Walton, Edward; Patel, Gool F.; Liang, Tehming; Cascieri, Margaret A.; Cheung, Anne H.; Brooks, Jerry R.; Berman, Charles
CORPORATE SOURCE: Dep. Biochem. Endocrinol., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(11), 2298-315
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:33371

AB A series of steroids, primarily 4-azasteroids, were prepared and tested in vitro as inhibitors of human and rat prostatic 5α-reductase and of binding of dihydrotestosterone to the rat androgen receptor. The primary structural modifications were changes of the A ring and of moieties attached at the C-17 positions of the steroid nucleus. New A-ring modifications included the 4-cyano-3-oxo-Δ4 system in the carbocyclic series and 1α-CN, 1α-CH3, 1α,2α-CH2, 2β-F, 2-aza, 2-oxa, or A-homo changes in the 3-oxo-4-aza series. In addition, 4-azasteroids with a D-homo ring or Me substitution at C-7 (α and β) or C-16 (α and β) were prepared The majority of the C-17 substituents were prepared from reactive intermediates derived from the 17β-COOH. Enhanced 5α-reductase inhibition in both the human and rat enzyme assays was seen with 4-CN substitution on 3-oxo-Δ4 steroids and with a C-17 side chain incorporating a lipophilically substituted semipolar group on the 4-aza-3-oxo-5α-androstane nucleus. Fewer highly active compds. were found in the human enzyme assay than in the rat assay. Structural requirements for inhibition of the rat androgen receptor were much different from those for inhibition of the enzyme. The 17β-OH moiety enhanced potency more than any other feature, whereas introduction of double bonds at C-1 or C-5 in the azasteroid gave a small improvement. Azasteroids unsubstituted at the 4-position demonstrated greatly diminished receptor activity.

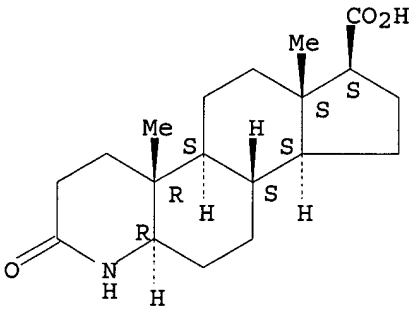
IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



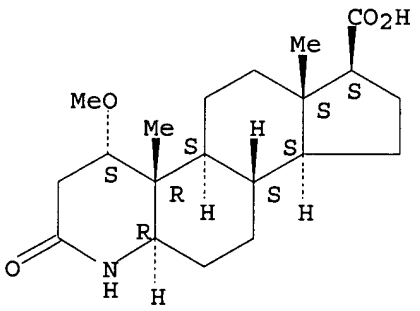
IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and methylation of)
RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **104215-28-3P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)
RN 104215-28-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4-methoxy-4a,6a-dimethyl-2-oxo-, (4S,4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/524,922

ACCESSION NUMBER: 1986:460814 CAPLUS
DOCUMENT NUMBER: 105:60814
TITLE: 17β-Substituted 4-aza-5α-androstenones and their use as testosterone 5α-reductase inhibitors
INVENTOR(S): Rasmusson, Gary H.; Reynolds, Glenn F.
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

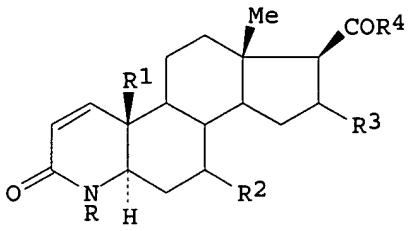
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 155096	A2	19850918	EP 1985-301122	19850220
EP 155096	A3	19860702		
EP 155096	B1	19891004		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 74365	A1	19900726	IL 1985-74365	19850218
IL 86924	A1	19900726	IL 1985-86924	19850218
EP 314199	A1	19890503	EP 1988-119105	19850220
EP 314199	B1	19910918		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 46912	E	19891015	AT 1985-301122	19850220
AT 67503	E	19911015	AT 1988-119105	19850220
AU 8539167	A1	19850905	AU 1985-39167	19850226
AU 584321	B2	19890525		
DK 8500859	A	19851022	DK 1985-859	19850226
DK 166704	B1	19930628		
ZA 8501426	A	19861029	ZA 1985-1426	19850226
ES 540705	A1	19870101	ES 1985-540705	19850226
CA 1314541	A1	19930316	CA 1985-475184	19850226
JP 60222497	A2	19851107	JP 1985-36714	19850227
JP 63065080	B4	19881214		
US 4760071	A	19880726	US 1985-800623	19851121
US 4859681	A	19890822	US 1987-129335	19871203
US 4822803	A	19890418	US 1988-152215	19880204
JP 01093600	A2	19890412	JP 1988-135348	19880601
JP 05041638	B4	19930624		
AU 8933135	A1	19890810	AU 1989-33135	19890418
AU 626293	B2	19920730		
AU 9170835	A1	19910711	AU 1991-70835	19910206
US 5120742	A	19920609	US 1991-683520	19910409
US 5138063	A	19920811	US 1991-701332	19910509
US 5151429	A	19920929	US 1991-764047	19910923
AU 9227481	A1	19930318	AU 1992-27481	19921030
AU 651741	B2	19940728		
US 5571817	A	19961105	US 1993-94815	19930720
US 5567708	A	19961022	US 1995-455464	19950531

PRIORITY APPLN. INFO.:		
US 1984-584061	A	19840227
US 1984-584062	A	19840227
US 1983-547508	A2	19831031
US 1984-661645	A2	19841017
IL 1985-74365	A	19850218
EP 1985-301122	P	19850220
EP 1988-119105	A	19850220
US 1985-725265	A3	19850419
US 1985-800623	A2	19851121
US 1985-800624	A1	19851121
US 1986-932549	B1	19861120
US 1987-1262	A3	19870107

US 1987-34806	B1	19870403
US 1987-129335	A1	19871203
US 1988-198708	B1	19880519
US 1988-285375	B1	19881216
US 1989-363567	B2	19890608
US 1989-370142	B1	19890621
US 1989-396183	B1	19890821
US 1990-536037	B1	19900611
US 1990-545676	B1	19900628
US 1990-630357	B1	19901218
US 1991-698374	B1	19910509
US 1992-927256	B1	19920807
US 1993-16476	B1	19930210
US 1993-94815	A1	19930720

OTHER SOURCE(S): CASREACT 105:60814; MARPAT 105:60814

GI



I

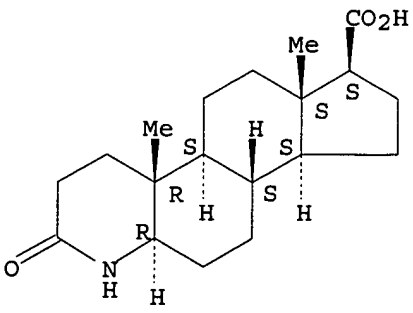
AB Azaandrostenones I [R = H, Me, Et; R1 = H, Me; R2, R3 = H, Me; R4 = R5, NHR5, R6; R5 = alkyl, (un)substituted monocyclic aryl; R6 = PhCH2, phenethyl, 2- or 4-pyridyl, 2-pyrrolyl, 2-furyl or thienyl] were prepared as testosterone 5α-reductase inhibitors for treatment of hyperandrogenic conditions (no data). Thus, Me 3-oxo-4-aza-5α-androstane-17-carboxylate was dehydrogenated by [PhSe(O)]2O to give azaandrostenone I (R = R2 = R3 = H, R1 = Me, R4 = OMe), which was N-methylated, saponified, and thioesterified with PPh3 and 2,2'-dipyridyl disulfide to give I (R = R1 = Me, R2 = R3 = H, R4 = 2-pyridylthio). Treatment of the thioester with anhydrous EtNH2 in THF gave I (R = R1 = Me, R2 = R3 = H, R4 = NHEt); treatment with sec-BuMgCl gave I (R = R1 = Me, R2 = R3 = H, R4 = sec-Bu).

IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and amidation of)

RN 103335-55-3 CAPLUS

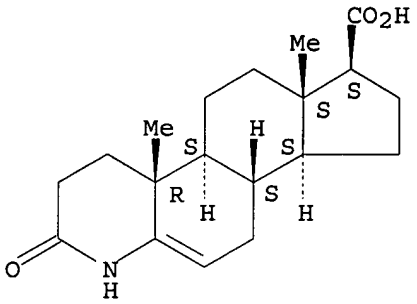
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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(FILE 'HOME' ENTERED AT 18:06:03 ON 30 JAN 2006)

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L2 2 S L1
L3 STRUCTURE UPLOADED
L4 0 S L3
L5 3 S L3 FULL
L6 14 S L1 FULL

FILE 'CAPLUS' ENTERED AT 18:08:21 ON 30 JAN 2006
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L9 17 S L7 AND L8

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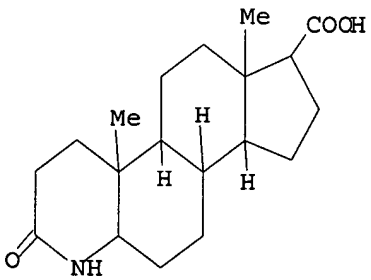
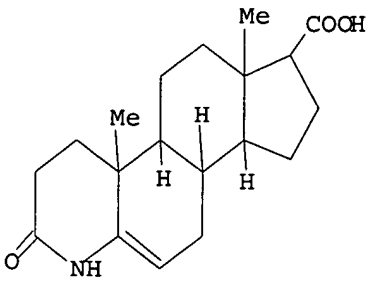
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> d l3
L3 HAS NO ANSWERS
L3 STR



Structure attributes must be viewed using STN Express query preparation.

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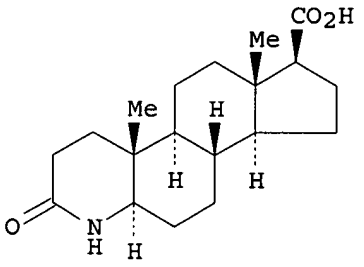
=> d ibib abs hitstr 1-2

L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:162674 CAPLUS
DOCUMENT NUMBER: 140:199498
TITLE: Method for the selective preparation of a 3-oxo-4-aza-5a-androstane derivative
INVENTOR(S): Moon, Young-ho; Lee, Kyung-ik; Park, Gha-seung; Park, Chul-hyun; Lee, Jae-cheol; Lee, Gwan-sun; Chang, Young-kil
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004016595	A1	20040226	WO 2003-KR1629		20030813
W: AU, CA, CN, HU, IN, JP, US					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
EP 1539703	A1	20050615	EP 2003-788151		20030813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK					
JP 2006501221	T2	20060112	JP 2004-528926		20030813
US 2006019979	A1	20060126	US 2005-524922		20050215
PRIORITY APPLN. INFO.:			KR 2002-48784	A	20020819
			WO 2003-KR1629	W	20030813

GI



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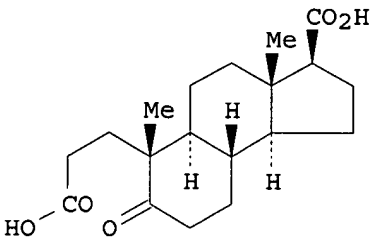


II

AB This invention relates to a method for selectively preparing 3-oxo-4-aza-5α-androstane derivative I, a precursor of finasteride, by heating 3-oxo-4-aza-5-androstene in a mixture of **formic acid** and an **alkanediol** in the presence of **zinc** . Thus, oxidative ring cleavage of 3-oxo-4-androstene-17β-carboxylic acid using sodium metaperiodate, potassium permanganate, and sodium carbonate in tert-butanol gave 3,5-secoandrostane II in 86% yield. Ring cleaved androstane II then underwent an intramol. cyclocondensation reaction by refluxing for 12 h using an ethanolic ammonia solution and ethylene glycol to form 3-oxo-4-aza-5-androstene-17β-carboxylic acid in 70% yield, which was subsequently hydrogenated by heating for 8 h at 100-105° using **formic acid**, ethylene glycol and **zinc** to give the desired finasteride precursor I in 81% yield.

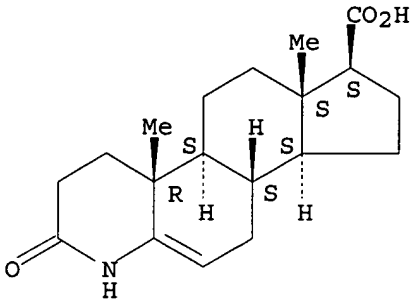
IT **103335-54-2P**, 3-Oxo-4-aza-5-androstene-17β-carboxylic acid
RL: IMF (Industrial manufacture); **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of 3-oxo-4-aza-5α-androstane, a finasteride

precursor, via a **zinc/formic acid/ alkanediol** mediated olefin hydrogenation)

RN 103335-54-2 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **103335-55-3P**, 3-Oxo-4-aza-5α-androstane-17β-carboxylic acid

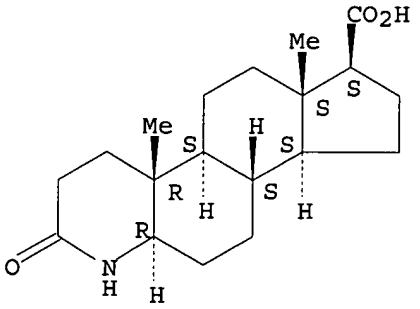
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**

(process for preparation of 3-oxo-4-aza-5α-androstane, a finasteride precursor, via a **zinc/formic acid/ alkanediol** mediated olefin hydrogenation)

RN 103335-55-3 CAPLUS

CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:33371 CAPLUS

DOCUMENT NUMBER: 106:33371

TITLE: Azasteroids: structure-activity relationships for inhibition of 5α-reductase and of androgen receptor binding

AUTHOR(S): Rasmusson, Gary H.; Reynolds, Glenn F.; Steinberg, Nathan G.; Walton, Edward; Patel, Gool F.; Liang, Tehming; Cascieri, Margaret A.; Cheung, Anne H.; Brooks, Jerry R.; Berman, Charles

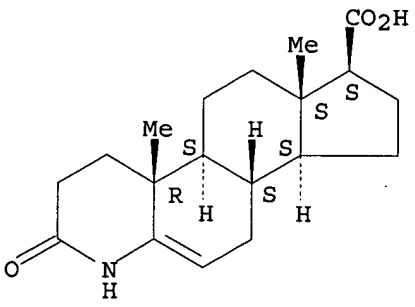
CORPORATE SOURCE: Dep. Biochem. Endocrinol., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA

SOURCE: Journal of Medicinal Chemistry (1986), 29(11), 2298-315
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:33371

AB A series of steroids, primarily 4-azasteroids, were prepared and tested in vitro as inhibitors of human and rat prostatic 5α-reductase and of binding of dihydrotestosterone to the rat androgen receptor. The primary structural modifications were changes of the A ring and of moieties attached at the C-17 positions of the steroid nucleus. New A-ring modifications included the 4-cyano-3-oxo-Δ4 system in the carbocyclic series and 1α-CN, 1α-CH3, 1α,2α-CH2, 2β-F, 2-aza, 2-oxa, or A-homo changes in the 3-oxo-4-aza series. In addition, 4-azasteroids with a D-homo ring or Me substitution at C-7 (α and β) or C-16 (α and β) were prepared The majority of the C-17 substituents were prepared from reactive intermediates derived from the 17β-COOH. Enhanced 5α-reductase inhibition in both the human and rat enzyme assays was seen with 4-CN substitution on 3-oxo-Δ4 steroids and with a C-17 side chain incorporating a lipophilically substituted semipolar group on the 4-aza-3-oxo-5α-androstane nucleus. Fewer highly active compds. were found in the human enzyme assay than in the rat assay. Structural requirements for inhibition of the rat androgen receptor were much different from those for inhibition of the enzyme. The 17β-OH moiety enhanced potency more than any other feature, whereas introduction of double bonds at C-1 or C-5 in the azasteroid gave a small improvement. Azasteroids unsubstituted at the 4-position demonstrated greatly diminished receptor activity.

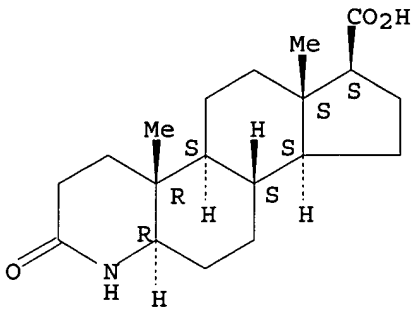
IT **103335-54-2P**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 103335-54-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, 2,3,4,4a,4b,5,6,6a,7,8,9,9a,9b,10-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **103335-55-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and methylation of)
RN 103335-55-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxylic acid, hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L2             1 S 103335-54-2/RN

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L4            23 S L2/RCT
L5            16 S L3 AND L4
L6        573201 S ZINC
L7             1 S L5 AND L6
L8         42287 S FORMIC ACID OR ALANEDIOL
L9         43532 S FORMIC ACID OR ALKANEDIOL
L10            2 S L5 AND L9
L11            2 S L7 OR L10

=> d re 1-5

L11  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
RE
(1) Glaxo Group Limited; US 4451405 A 1984 CAPLUS
(2) Glaxo Group Limited; WO 0246207 A2 2002 CAPLUS
(3) Peng, X; Heterocycles 1998, V47(2), P703
(4) Research Corporation Technologies Inc; US 5804576 A 1998 CAPLUS
(5) Templeton, J; J Chem Soc Perkin Trans 1 1990, V9, P2581

L11  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN


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